



**UNITED STATES DEPARTMENT OF COMMERCE  
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/252,828	02/19/99	DONG	K 024754/0114

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HM22/0509

EXAMINER

COOK, L

ART UNIT	PAPER NUMBER
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1641

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DATE MAILED:

05/09/00

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

# Office Action Summary

Application No.  
09/252,828

Applicant(s)  
Dong et al.

Examiner  
Lisa V. Cook

Group Art Unit  
1641



☒ Responsive to communication(s) filed on Mar 30, 2000

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1035 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

## Disposition of Claim

☒ Claim(s) 1, 2, and 6-24 is/are pending in the application

Of the above, claim(s) 12-21 is/are withdrawn from consideration

☐ Claim(s) \_\_\_\_\_ is/are allowed.

☒ Claim(s) 1, 2, 6-11, and 22-24 is/are rejected.

☒ Claim(s) 2 is/are objected to.

☒ Claims 1, 2, and 6-24 are subject to restriction or election requirement.

## Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on \_\_\_\_\_ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some\* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 5 and 6

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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## **DETAILED ACTION**

### ***Election/Restriction***

1. Applicant's election of Group I, claims 1-2, 6-11, and 22-24, for prosecution in the subject application is acknowledged. Because Applicant did not distinctly and specifically points out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

In response to the Preliminary Amendment filed 10 March 2000 (Paper #8), Claims 3-5 have been cancelled without prejudice or disclaimer. New claims (22-24) drawn to the method of producing the specific glycoprotein in the invention of Group I, were added.

2. Currently, Claims 1-2, 6-11, and 22-24 are pending and under consideration.

### ***Priority***

3. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78). This application does not contain the required first sentence of the specification referencing the provisional priority document 60/075,079 filed 12/19/98. Please add to the specification.

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***Drawings***

4. The drawings in this application are objected to by the Draftsperson under 37 CFR 1.84 or 1.152 (see PTO-948).

***Information Disclosure Statement***

5. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the examiner on form PTO-892 or applicant on form 1449 has cited the references they have not been considered.

***Oath/Declaration***

6. A new oath or declaration is required because the date inventor Ke-Wen Dong signed the oath/Declaration is not provided. The wording of an oath or declaration cannot be amended. If the wording is not correct or if all of the required affirmations have not been made or if it has not been properly subscribed to, a new oath or declaration is required. The new oath or declaration must properly identify the application of which it is to form a part, preferably by application number and filing date in the body of the oath or declaration. See MPEP §§ 602.01 and 602.02.

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### ***Specification***

7. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

The abstract of the disclosure is objected to because it is not clear as to what the abbreviation "Id." is meant to designate. (See page 3, line 24,) Is this intended to refer to the previously mention reference of Beebe et al. recited on page 3, line 16.

Clarification is required. See MPEP § 608.01(b).

### ***Claim Objections***

8. Claim 2 is objected to because of the following informalities: The claim refers to the "glycoprotein" of claim 1, while claim 1 and all other claims in the instant application recite a "glycopolypeptide". Although it is recognized that the terms could be utilized interchangeable, it is suggested that one term be consistently employed for clarity.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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9. Claims 1-2, 6-11, and 22-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 1 and 22 are vague and indefinite because it is unclear as to what the term "acrosome reaction" entails. The claim recites a glycopolypeptide that can strongly bind human spermatozoa and induce an acrosome reaction in the spermatozoa. Because the term is not defined in the disclosure, the metes and bound of the claim can not be determined. Is it applicant's intent to define any event involving a spermatozoon that releases an egg-penetrating enzyme? Please define.

B. Claim 1 and 22 are vague and indefinite because it is unclear as to what the term "acrosome reaction" entails. The claim recites a glycopolypeptide that can strongly bind human spermatozoa and induce an acrosome reaction in the spermatozoa. Because the term is not defined in the disclosure, the metes and bound of the claim can not be determined. Is it applicant's intent to define any event involving a spermatozoon that releases an egg-penetrating enzyme? Please define.

C. In claim 2, the use of "produced by" is vague and indefinite. The term produced implies any form of production from the cell including natural and synthetic means. The claim could recite -(The glycoprotein of claim 1, wherein a transduced/transfected human ovarian cell line produces the glycoprotein). Another possibility is to utilize the term "expressed by" be in the claim for clarity.

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D. Claim 6 is vague and indefinite because it is unclear if the glycopolypeptide binds to human sperm or not? The use of the term "preferentially binds" renders the claim indefinite.

E. Claim 6 recites the limitation "predicted". The recited claim is unclear and indefinite because it is not known if the O-glycosylation site is one that is known in the art per se or any site that can be shown to be an adequate O-glycosylation site. Further, it is not known what would constitute a predictive O-glycosylation site (i.e. binds 100% or >90%). Please explain.

F. Claims 23 and 24 are vague and indefinite in the use of the acronyms hZP3 and PA-1. The terms should be defined in their first instance. This initial explanation will convey intended meaning with subsequent abbreviations. Please define.

### ***Inventive Conclusion***

10. The present invention is directed to the production and utility of a purified recombinant human zone pellucida protein 3 (HZP3), which is expressed in an ovarian cell line and employed to detect male fertility.

### ***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain patent therefor, subject to the conditions and requirements of this title.

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11. Claims 2 and 6-11 are directed to non-statutory subject matter. There is no recitation of isolation or purification. Therefore, the claimed glycoprotein and/or glycopolypeptide read on naturally occurring materials, which are considered to be non-statutory and non-patentable subject matter within the scope of 35 U.S.C. 101. See Official gazette, 1077 O.G. 24, April 21, 1987. It is recommended that the claims incorporate the claim language, "isolated or purified" to overcome this rejection.

***Claim Rejections - 35 USC § 102***

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

I. Claims 1,2, 6-11, and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Van Duin (WO 92/03548).



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Van Duin disclosed a polypeptide and functional derivatives thereof which have human ZP3 activity or human ZP3 antigenicity. The polypeptides can be produced either synthetically or by recombinant DNA technology. Specifically, the polypeptide to be expressed is coded for by a DNA sequence or more accurately a nucleic acid sequence. The nucleic acid sequence is optionally transcribed and translated to the target polypeptide via cloning into a vector transformed into a host cell. The vector may be self-replicating or it may integrate into the DNA of the host. (See page 2)

Different host cells can lead to different polypeptides. (Prokaryotes are not adapted for glycosylation, Eukaryotes have the means of glycosylation, but yeast cells give a different glycosylation pattern than mammalian cells). Since the inventors were concerned with human glycoprotein production all of their research included mammalian cell hosts. The resulting glycopolypeptides produced in this invention comprised several amino acid lengths (i.e. 41 to 400) and they were found to be 92% homologous with the instant invention product in SEQ ID NO:1. (MPSRCH comparing protein-protein database search utilizing Smith-Waterman algorithm - A).

II. Claims 1,2, 6-11, and 22 are rejected under #5 U.S.C. 102(b) as being anticipated by Harris et al. (WO 94/11019).

Harris et al. teach methods related to the purification and isolation of DNA sequences encoding the zona pellucida proteins from various mammalian species. The zona pellucida is a complex matrix surrounding the mammalian oocyte, formed of

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glycoproteins secreted by ovarian cells. Zone pellucida (ZP) glycoproteins perform a number of different functions. For example, the mouse ZP has been shown to provide structural integrity to the matrix, to be a sperm receptor in the matrix, to induce the sperm acrosome reaction on the surface of ZP, and to maintain binding between the sperm/egg as a secondary receptor. (Page 1 and Page 2) In example 11, Harris et al. isolate and purify a human DNA sequences encoding human zona pellucida proteins ZPA and ZPB. These glycoprotein structures were found to be 92.6% homologous to the instant inventive products. (MPSRCH comparing protein-protein database search utilizing Smith-Waterman algorithm - A).

III. Claims 1,2, 6-11, and 22 are rejected under #5 U.S.C. 102(e) as being anticipated by Harris (U.S.Patent#5,837,497).

Harris et al. teach methods related to the purification and isolation of DNA sequences encoding the zona pellucida proteins from various mammalian species. The zona pellucida is a complex matrix surrounding the mammalian oocyte, formed of glycoproteins secreted by ovarian cells. Zone pellucida (ZP) glycoproteins perform a number of different functions. For example, the mouse ZP has been shown to provide structural integrity to the matrix, to be a sperm receptor in the matrix, to induce the sperm acrosome reaction on the surface of ZP, and to maintain binding between the sperm/egg as a secondary receptor. (Column 1, Lines 24-52) In example 11, Harris et al. isolate and purify a human DNA sequences encoding human zona pellucida

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proteins ZPA and ZPB. These glycoprotein structures were found to be 92.6% homologous to the instant inventive products. (MPSRCH comparing protein-protein database search utilizing Smith-Waterman algorithm - A).

***Claim Rejections - 35 USC § 103***

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

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I. Claims 23 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Van Duin (WO 92/03548), Harris et al. (WO 94/11019) or Harris (U.S. Patent #5,837,497) in view of Chamberlin et al. (Proc. Natl. Acad. Sci. USA, Developmental Biology, Vol. 87, pp. 6014-6018, August 1990) and in further view of Stern et al. (U.S. patent #5,869,053).

Please see previous discussions of Van Duin, Harris et al., and Harris.

Van Duin, Harris et al., and Harris differ from the instant invention in not identifying the specific full-length structure of Human ZP3 cDNA and the specific transducing cell line of the PA-1.

However, Chamberlin et al. disclose this limitation in the reference found in the Proc. Natl. Acad. Sci. USA, Developmental Biology, Vol. 87, pp. 6014-6018, August 1990. The full-length was previously established in this teaching. Chamberlin et al. take advantage of the cross-hybridization of the mouse cDNA and human DNA to isolate and characterize the full-length cDNA clones of human ZP3 (deposited in the GenBank data base-accession no. M35109). Human ZP3 cDNA was purified from total RNA isolated from a human ovary and used as the first-strand synthesis with oligonucleotide primer A2T15. The first-strand was amplified by PCR.

Further, the utility of the PA-1 (human ovarian carcinoma) cell line in PCR techniques involving glycoproteins was also established. In the patent of Stern et al. the glycoprotein 5T4 was identified in human trophoblast. In table III, the reactivity of MAB 5T4 with normal cells and transformed cell lines in cell-surface immunofluorescence and

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radiobinding assays showed a comparatively high binding index (4.9 in the Ovary cell PA-1. A comparison of reactivity with negative control xenogeneic cell lines indicated positive expression of the antigen. (Column 8, lines 52-61)

Van Duin, Harris et al., Harris, Chamberlin et al., and Stern et al. are analogous art because they are from the same field of endeavor, all the cited inventions teach method involving glycoprotein production and isolation techniques.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the ovarian cell line PA-1 and human ZP3 as taught by Chamberlin et al., and Stern et al. in either method of Van Duin, Harris et al., or Harris to perform glycoprotein production via the transduction of a human ovarian cell line with a polynucleotide that encodes a polypeptide comprising ZP3 because such methods of evaluation as taught by Van Duin, Harris et al., or Harris is well known in the art. A person of ordinary skill in the art would have had a reasonable expectation of success utilizing such techniques, because both the PA-1 cell line and the full-length human ZP3 sequence were established in the prior art.

The motivation to utilize such compounds can be found in the predictable glycosylation sites of ZP3 and its homology to the mouse analogue, which has strong binding affinity for spermatozoa and induces an acrosome reaction.

14. For reasons aforementioned, no claims are allowed.

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**Remarks**

15. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

A. Ozgur et al. (Molecular Human Reproduction, Vol.4, No.4, pp.318-324, 1998) teach direct evidence of the binding process dependency upon the recognition of oligosaccharides sequences associated with zona pellucida glycoproteins.

B. Mes-Masson et al. (U.S.Patent#5,710,038) disclose methods of producing primary culture of normal human ovarian epithelium.

C. Dean (U.S.Patent#'s, 5,626,846-5,641,487-5,672,488-5,916,768) teach contraceptive vaccines based on cloned zona pellucida genes and zona pellucida polypeptides.

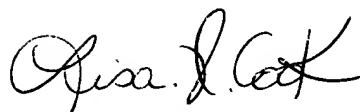
16. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 Fax number is (703) 308-4242, which is able to receive transmissions 24 hours/day, 7 days/week.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (703) 305-0808. The examiner can normally be reached on Monday-Friday from 8:00 AM - 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.



*Lisa V. Cook*

*CM1-7D16*

*(703) 305-0808*

*05/05/00*



JAMES C. HOUSEL 5/8/00  
SUPERVISORY PATENT EXAMINER